

**EXPRESS MAIL #EL822582809US***Application No.: PCT/US00/19336*

interleukin-10 (IL-10) or an interferon, and an active variant thereof, wherein the immunoglobulin domain does not contain a variable region, and wherein the soluble protein and the immunoglobulin domain are joined by a peptide linker that is not AspProGlu or Ser.

3. (Reiterated) The fusion protein of claim 2, wherein the peptide linker is SerGly.

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4. (Once Amended) The fusion protein of claim 2, wherein the peptide linker is Ser(GlyGlySer)<sub>n</sub> (SEQ ID NO:1), wherein n is 1 to 7.

5. (Once Amended) The fusion protein of claim 2, wherein the peptide linker is SerGlyGlySer (SEQ ID NO:1) or Ser(GlyGlySer)<sub>2</sub> (SEQ ID NO:3).

6. (Once Amended) The fusion protein of Claim 1, wherein the Ig domain is selected from the group consisting of IgG-Fc, IgG-C<sub>H</sub> and IgG-C<sub>L</sub>.

7. (Once Amended) The fusion protein of Claim 1, wherein the soluble protein is a member of the growth hormone (GH) supergene family.

8. (Once Amended) The fusion protein of Claim 1, wherein the soluble protein is granulocyte-colony stimulating factor (G-CSF).

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9. (Reiterated) The fusion protein of claim 8, wherein the fusion protein has an EC<sub>50</sub> of less than about 300 ng/ml in a G-CSF-dependent cell assay.

10. (Reiterated) The fusion protein of claim 8, wherein serine is substituted for cysteine-17 of G-CSF.

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12. (Once Amended) The fusion protein of Claim 1, wherein the soluble protein is growth hormone (GH).

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14. (Once Amended) The fusion protein of Claim 1, wherein the soluble protein is selected from the group consisting of granulocyte-macrophage colony stimulating factor (GM-CSF), interleukin-11 (IL-11), thrombopoietin (TPO), stem cell factor (SCF) and flt3 ligand.

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15. (Reiterated) A homomultimeric fusion protein comprising two or more copies of a member of the Growth Hormone (GH) supergene family joined without an intervening peptide linker.

16. (Reiterated) A homomultimeric fusion protein comprising two or more copies of a member of the Growth Hormone (GH) supergene family joined by at least one peptide linker, wherein the member of the GH supergene family is selected from the group consisting of: growth hormone, prolactin, placental lactogen, thrombopoietin (TPO), interleukin(IL)-2, interleukin-3, interleukin-4, interleukin-5, interleukin-6, interleukin-7, interleukin-9, interleukin-10, interleukin-11, interleukin-12 (p35 subunit), interleukin-13, interleukin-15, oncostatin M, ciliary neurotrophic factor, leukemia inhibitory factor, alpha interferon, beta interferon, gamma interferon, omega interferon, tau interferon, granulocyte-colony stimulating factor (G-CSF), granulocyte-macrophage colony stimulating factor (GM-CSF), cardiotrophin-1, macrophage colony stimulating factor, Stem Cell Factor and flt-3 ligand.

216 17. (Once Amended) The homomultimeric fusion protein of Claim 15, wherein the member of the GH supergene family is granulocyte-colony stimulating factor (G-CSF).

18. (Reiterated) The homomultimeric fusion protein of claim 17, wherein the homomultimeric fusion protein is a dimeric G-CSF fusion protein.

19. (Reiterated) The homomultimeric fusion protein of Claim 15, wherein the member of the GH supergene family is EPO.

20. (Once Amended) The homomultimeric fusion protein of Claim 19, wherein the multimeric fusion protein is a dimeric EPO fusion protein.

217 21. (Once Amended) The homomultimeric fusion protein of Claim 15, wherein the member of the GH supergene family is selected from the group consisting of: growth hormone, alpha interferon, beta interferon, gamma interferon, GM-CSF, IL-11, TPO, SCF, and Flt3 ligand.

22. (Once Amended) The fusion protein of Claim 16, wherein the peptide linker is SerGly.

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23. (Once Amended) The fusion protein of Claim 16, wherein the peptide linker is Ser(GlyGlySer)<sub>n</sub> (SEQ ID NO:1), wherein n is 1 to 7.

24. (Once Amended) The fusion protein of Claim 1, wherein said fusion protein is dimeric and is essentially free of monomeric fusion protein.

25. (Once Amended) The fusion protein of claim 24, wherein the soluble protein is selected from the group consisting of G-CSF, EPO and interleukin-11.

26. (Once Amended) A method of producing a fusion protein of Claim 2, comprising:

- a. transfecting or transforming a host cell with at least one nucleic acid encoding the fusion protein of Claim 2;
- b. culturing the host cell; and
- c. harvesting the fusion protein expressed by the host cell.

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27. (Reiterated) The method of claim 26, wherein the nucleic acid further encodes a peptide linker.

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28. (Once Amended) A nucleic acid encoding the fusion protein of Claim 1.

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29. (Reiterated) A host cell transfected or transformed with the nucleic acid of claim 28, enabling the host cell to express the fusion protein.

30. (Reiterated) The host cell of claim 29, wherein the host cell is a eukaryotic cell.

31. (Reiterated) The host cell of claim 30, wherein the eukaryotic cell is a mammalian cell.

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32. (Once Amended) A method of purifying the fusion protein of Claim 1, comprising:

- a. obtaining a composition comprising the fusion protein; and
- b. isolating the fusion protein from contaminants by column chromatography.

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33. (Reiterated) The method of claim 32, wherein the fusion protein is isolated from contaminants by size-exclusion chromatography.

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34. (Once Amended) A method of treating a condition treatable with a member of the Growth Hormone (GH) supergene family, comprising administering an effective amount of the fusion protein of Claim 1 to a patient in need thereof.

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35. (Reiterated) The method of claim 34, wherein the fusion protein is a G-CSF-Immunoglobulin fusion protein and wherein the condition is a deficiency of blood neutrophils.

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36. (Reiterated) The method of claim 34, wherein the fusion protein is an EPO-Immunoglobulin fusion protein and wherein the condition is a deficient hematocrit.

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37. (Once Amended) A pharmaceutical composition comprising the fusion protein of Claim 1 in a pharmaceutically acceptable carrier.

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38. (Once Amended) The fusion protein of Claim 1, wherein the soluble protein is erythropoietin (EPO).

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39. (Reiterated) The fusion protein of Claim 1, wherein the soluble protein is selected from the group consisting of alpha interferon, beta interferon, gamma interferon, omega interferon and tau interferon.

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40. (Reiterated) A homomultimeric fusion protein, comprising two or more copies of erythropoietin joined by at least one peptide linker, wherein the peptide linker is not Gly<sub>3-7</sub>.

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41. (Reiterated) A multimeric fusion protein comprising two or more different members of the Growth Hormone supergene family joined by at least one peptide linker, wherein the members of the Growth Hormone supergene family are selected from the group consisting of growth hormone, prolactin, placental lactogen, erythropoietin (EPO), thrombopoietin (TPO), interleukin(IL)-2, interleukin-4, interleukin-5, interleukin-6, interleukin-7, interleukin-9, interleukin-10, interleukin-11, interleukin-12 (p35 subunit), interleukin-13, interleukin-15, oncostatin M, ciliary neurotrophic factor, leukemia inhibitory factor, alpha interferon, beta interferon, gamma interferon, omega interferon, tau interferon,

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granulocyte-colony stimulating factor (G-CSF), cardiotrophin-1, macrophage colony stimulating factor, Stem Cell Factor and flt-3 ligand.

42. (Once Amended) The method of Claim 26, further comprising purifying dimeric fusion protein from monomeric fusion protein.

Please add the following new Claims 43-61.

43. (Added) A method of producing a fusion protein of Claim 1, comprising:

- a. transfecting or transforming a host cell with at least one nucleic acid encoding the fusion protein of Claim 1;
- b. culturing the host cell; and
- c. harvesting the fusion protein expressed by the host cell.

44. (Added) The fusion protein of Claim 2, wherein the soluble protein is erythropoietin (EPO).

45. (Added) The fusion protein of Claim 2, wherein the Ig domain is selected from the group consisting of IgG-Fc, IgG-C<sub>H</sub> and IgG-C<sub>L</sub>.

46. (Added) The fusion protein of Claim 2, wherein the soluble protein is a member of the growth hormone (GH) supergene family.

47. (Added) The fusion protein of Claim 2, wherein the soluble protein is granulocyte-colony stimulating factor (G-CSF).

48. (Added) The fusion protein of Claim 47, wherein the fusion protein has an EC<sub>50</sub> of less than about 300 ng/ml in a G-CSF-dependent cell assay.

49. (Added) The fusion protein of Claim 47, wherein serine is substituted for cysteine-17 of G-CSF.

50. (Added) The fusion protein of Claim 2, wherein the soluble protein is growth hormone (GH).

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51. (Added) The fusion protein of Claim 2, wherein the soluble protein is selected from the group consisting of granulocyte-macrophage colony stimulating factor (GM-CSF), interleukin-11 (IL-11), thrombopoietin (TPO), stem cell factor (SCF) and flt3 ligand.

52. (Added) The fusion protein of Claim 2, wherein said fusion protein is dimeric and is essentially free of monomeric fusion protein.

53. (Added) The fusion protein of claim 52, wherein the soluble protein is selected from the group consisting of G-CSF, EPO and interleukin-11.

54. (Added) The homomultimeric fusion protein of Claim 16, wherein the member of the GH supergene family is granulocyte-colony stimulating factor (G-CSF).

55. (Added) The homomultimeric fusion protein of claim 54, wherein the homomultimeric fusion protein is a dimeric G-CSF fusion protein.

56. (Added) The homomultimeric fusion protein of Claim 16, wherein the member of the GH supergene family is selected from the group consisting of: growth hormone, alpha interferon, beta interferon, gamma interferon, GM-CSF, IL-11, TPO, SCF, and Flt3 ligand.

57. (Added) The homomultimeric fusion protein of Claim 40, wherein the multimeric fusion protein is a dimeric EPO fusion protein.

58. (Added) The fusion protein of Claim 40, wherein the peptide linker is SerGly.

59. (Added) The fusion protein of Claim 40, wherein the peptide linker is Ser(GlyGlySer)<sub>n</sub> (SEQ ID NO:1), wherein n is 1 to 7.

60. (Added) The fusion protein of Claim 41, wherein the peptide linker is SerGly.

61. (Added) The fusion protein of Claim 41, wherein the peptide linker is Ser(GlyGlySer)<sub>n</sub> (SEQ ID NO:1), wherein n is 1 to 7.

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